Abstract

Poor-quality medicines are real threats to individuals and health systems worldwide. In developing countries, life-saving medicines, such as antibiotics, are the main target of counterfeiters. Substandard medicines are extremely prevalent due to poor manufacturing, distribution, and/or storage conditions. Data on the quality of medicines in Arab countries are very limited. This thesis is divided into two major parts.

The first part investigated the quality of amoxicillin capsules and tablets sold in community pharmacies (CPs) in Riyadh, Saudi Arabia, as an indicator of the quality of medicines sold in them. It estimated the proportion of pharmacies that were selling poor-quality medicines relative to a predetermined threshold (20%). It also field tested an economical sampling method for classifying the CPs according to the quality of their medicines in order to help decision makers with resource allocation.

Sampling was performed with the “mystery shopper” technique in 72 randomly selected CPs in Riyadh. The number of pharmacies for inclusion was calculated with Lot Quality Assurance Sampling (LQAS) method. The initial 1367 pharmacies were divided into two lots: chain and independent pharmacies (869 and 498, respectively). From each lot, 36 pharmacies were randomly selected, and 80 dosage units of a randomly selected amoxicillin brand were purchased from each selected pharmacy. If this brand was from more than one batch, the batches were considered different samples purchased from the same pharmacy. If samples from the same batch were purchased from different pharmacies, the samples were also considered different. The samples were checked for authenticity and analyzed for their drug content and content uniformity (CU) according to the United States Pharmacopeia (USP) by a validated high-performance liquid chromatographic (HPLC) method. If a sample from a pharmacy was found to be of poor quality, that pharmacy was considered a failed

pharmacy. If the number of failed pharmacies exceeded a predetermined decision value (three) in any lot, the lot was rejected and the proportion of pharmacies selling poor-quality amoxicillin was classified as higher than the predetermined threshold.

A total of 83 samples from 72 pharmacies were collected and analyzed (41 samples from chain pharmacies and 42 from independent pharmacies). The samples were found to be authentic, but 9 were substandard because they failed the CU test, with 6 of the 9 averaging less than 90% of the labeled content (the lowest was 80.7%). The content of the approved samples ranged from 90.6% to 104.2%. Certain batches passed the test in certain pharmacies and failed in others, indicating a possible degradation. The 9 failed samples were purchased from 4 chain and 5 independent pharmacies. Both lots were rejected because the predetermined decision value was exceeded, indicating that more than 20% of the pharmacies in each lot were selling poor-quality amoxicillin.

A problem existed with the quality of an essential drug in Riyadh's CPs. Exposure to excessive temperature during distribution or storage has unfavorable consequences on the quality of medicines, particularly in hot climates. This could be one of the possible reasons behind the existence of substandard amoxicillin in Riyadh's CPs. However, inefficient quality control at the manufacturing stage cannot be excluded.

The second part of the thesis explored the conditions under which medicines were kept in a random sample of 181 CPs in Riyadh. The pharmacist in charge in each pharmacy was interviewed and observations about the quality of storage were recorded.

The inspection revealed that in 9% of the CPs the readings of the existing room thermometers were more than 25 °C, and that 13% of the CPs lacked thermometers. Also in 33% of the CPs the readings of the refrigerator thermometers were outside the accepted range, and 7% of the CPs lacked refrigerator thermometers. About 15% of pharmacists were not informed about the local regulations of community pharmacy

practice, neither before nor after taking up their current positions. Surprisingly, incorrect answers to simple questions about the system were frequently given by the informed pharmacists. Certain aspects of substandard storage conditions existed, in varying degrees, in significant percentages of pharmacies regardless of the pharmacists' qualifications, experience, or awareness about the local regulations of community pharmacy practice.

Stricter monitoring of the supply chain in Riyadh is necessary. More studies to monitor the quality of medicines and pharmacies are recommended, together with improvements in the education of pharmacists and distributors about the importance of adhering to optimal conditions of keeping and selling medicines.

学位論文審査結果の要旨

KHOJAH HANI MAHMOUD J 氏は初めて、Lot Quality Assurance Sampling (LQAS) 法を医薬品の品質に関するフィールド調査に応用した。市場に流通している医薬品の品質評価は、ランダムサンプリングでは数千から数万のサンプルサイズとなり、その品質分析は現実的でなく、また、偽造薬に関しては、母集団の蔓延実態も不明である。これまでほとんどの調査が convenience sampling で行われている。HANI 氏は薬局評価の指標として販売医薬品の品質測定を行うという画期的な着想により、72 店舗からアモキシシリン（偽造ターゲット薬の一つ）を収集し分析した。その結果、リヤド市では品質不良のアモキシシリンを販売する薬局が許容範囲を超えており、指導の強化やさらなる品質調査の必要性を結論づけた。この方法は、不良薬や偽造薬の割合を示すものではないが、効率よく、販売薬の品質問題の存在を示す方法として極めて有益であり、大きな価値がある。

さらに、同一ロット番号のアモキシシリンでも、品質適合品と不良品があったことから、ランダムサンプリングしたリヤドの薬局の構造的面接と観察により、医薬品の貯蔵が不適切なものが薬剤師の資格や経験、GPP の認識に関わらず相当数存在することを明らかにした。当局による指導強化は医薬品の保管条件と薬剤師の生涯教育が重要であることを示した。

HANI 氏の二つの研究は、流通医薬品の品質確保に、有意義な手法を示したものであり、博士号に相応しい成果である。